SIRT3 Reverses Aging-Associated Degeneration.

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Public Summary:
Mitochondria are organelles that supply energy necessary for many cellular functions. SIRT3 protects against damage done to mitochondria by oxygen radials, and is present in high concentration in hematopoietic (blood-forming) stem cells. Here we show that SIRT3 is necessary for hematopoietic stem cells' ability to replenish blood cells in aged animals or animals of any age under physiological stress. SIRT3 is suppressed with aging, and hematopoietic stem cell function also decreases with age. Our study shows that up-regulation of SIRT3 in aged hematopoietic stem cells improves their regenerative capacity, reversing aging-associated degeneration.

Scientific Abstract:
Despite recent controversy about their function in some organisms, sirtuins are thought to play evolutionarily conserved roles in lifespan extension. Whether sirtuins can reverse aging-associated degeneration is unknown. Tissue-specific stem cells persist throughout the entire lifespan to repair and maintain tissues, but their self-renewal and differentiation potential become dysregulated with aging. We show that SIRT3, a mammalian sirtuin that regulates the global acetylation landscape of mitochondrial proteins and reduces oxidative stress, is highly enriched in hematopoietic stem cells (HSCs) where it regulates a stress response. SIRT3 is dispensable for HSC maintenance and tissue homeostasis at a young age under homeostatic conditions but is essential under stress or at an old age. Importantly, SIRT3 is suppressed with aging, and SIRT3 upregulation in aged HSCs improves their regenerative capacity. Our study illuminates the plasticity of mitochondrial homeostasis controlling stem cell and tissue maintenance during the aging process and shows that aging-associated degeneration can be reversed by a sirtuin.